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Heart Failure

INTERLEUKIN 23 REDUCES MYOCARDIAL INFLAMMATION AND IMPROVES INFARCT HEALING AFTER EXPERIMENTAL MYOCARDIAL INFARCTION BY CONTROLLING THE FUNCTION OF CARDIAC FIBROBLASTS

Poster Contributions

Poster Sessions, Expo North

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Authors: *Konstantinos Savvatis, Kathleen Pappritz, Dirk Westermann, Peter-Moritz Becher, Heinz-Peter Schultheiss, Carsten Tschöpe, Department of Cardiology, Charité Universitätsmedizin Berlin, Berlin, Germany*

Background: Interleukin 23 coordinates together with other cytokines the adaptive immune response with important effects on neutrophils, Th17 and regulatory T cells. The IL-23/Th17 axis is upregulated in several myocardial diseases. We sought to determine the role of IL-23 in experimental myocardial infarction (MI).

Methods: MI was induced by ligation of the left anterior descending artery in C57Bl6j and IL-23 knockout mice. Left ventricular (LV) function was examined by conductance catheter, expression of cytokines and collagen by RT-PCR and inflammatory cells in the myocardium by immunohistochemistry after 4 and 30 days. Differentiation and phenotype of cardiac fibroblasts was assessed under basal conditions and after stimulation with interferon- γ (IFN γ).

Results: Expression of IL-1 β was upregulated by 50% ($p=0.006$) and IFN γ by 100% ($p=0.05$) in the infarction zone in the IL-23-knockout mice. Migration of neutrophils and macrophages in the infarcted area was higher in the IL23-knockout mice (by 43%, $p=0.04$ and 41%, $p=0.03$ respectively). IL-23-knockout mice showed a lower 30-days survival rate due to increased ventricular rupture (63% vs. 24%, $p=0.036$) and a progressive LV-dilation already 4 days after MI (30% higher endystolic, $p=0.05$ and 35% higher enddiastolic LV-volume, $p=0.02$). Expression of α -smooth muscle actin (α -SMA, 2fold increase, $p<0.05$), collagen I (2.1fold increase, $p<0.05$) and III (1.9fold increase, $p<0.01$) as markers of fibrosis and activation of myofibroblasts were significantly higher in the infarction area in the wild type mice 30 days after infarction. Cardiac fibroblasts isolated from the infarcted and non-infarcted zones showed a 50% lower expression of α SMA, 30% lower collagen I and 20% lower collagen III ($p<0.05$) in the IL23KO-mice. Stimulation of cardiac fibroblasts with IFN γ led to a downregulation of α SMA and collagen I and upregulation of the proinflammatory chemokines CCL2 and CXCL10.

Conclusion: IL23 controls the expression of IFN γ in the heart after MI and induces differentiation of cardiac fibroblasts into myofibroblasts promoting healing and wound stabilization.